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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/564,620	01/13/2006	Pninna Fishman	FISHMAN18A	1534

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EXAMINER	
HENRY, MICHAEL C	
ART UNIT	PAPER NUMBER
1623	
MAIL DATE	DELIVERY MODE
12/01/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/564,620	FISHMAN ET AL.	
	Examiner	Art Unit	
	MICHAEL C. HENRY	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 August 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,5-10 and 20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 2, 5-10 and 20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The following office action is a responsive to the Amendment filed, 08/19/08

The amendment filed 08/19/08 affects the application, 10/564,620 as follows:

1. Claims 1, 8 have been amended. Claims 3-4 have been canceled. New Claims 20 has been added. Upon further consideration, it was determined that the indication of allowable subject matter in the office action mailed 01/25/08, was not appropriate. Consequently the said allowable subject matter is withdrawn. The rejections made under 35 U.S.C. 103(a) is maintained.
2. The responsive to applicants' amendment and arguments is contained herein below. Claims 1, 2, 5-10 and 20 are pending in the application.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 2, 5-10, 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fishman (WO2004/045627 A1).

In claim 1, applicant claims a method for the treatment of accelerated bone resorption that is not induced by inflammation, in a mammal subject, the method comprising administering to said subject in need of said treatment an amount of an A3 adenosine receptor agonist (A3AR agonist), the amount being effective to inhibit bone resorption. Claims 2, 5-6 are drawn said

method, wherein the subject is human, the administration is oral, the A_3AR agonist is administered specific times per day and the use of specific A_3AR agonist including IB-MECA and Cl-IB-MECA. Claim 7 is drawn to a method of claim 1 wherein said A_3AR agonist is a compound within the scope of a given general formula (I). Claim 8 is drawn to the method of claim 1, wherein said A_3AR agonist is a nucleoside derivative of a given general formula (IV). Claims 9-10 are drawn to said method involving specific A_3AR agonist including IB-MECA and Cl-IB-MECA. Claim 20 is drawn to the method of claim 1, wherein said subject is other than one suffering from an inflammatory arthritis.

Fishman discloses a method of treating inflammatory arthritis comprising administering to a subject an A_3 adenosine receptor agonist (A_3AR agonist) (see abstract and claims). Furthermore, Fishman discloses uses the A3 receptor agonists IB-MECA and Cl-IB-MECA for the said treatment (see abstract and claims). Also, Fishman reduces the bone loss (bone resorption) in a subject by administering to the subject IB-MECA. In addition, Fishman measures the loss of bone and reports that bone loss was markedly lower in the subjects treated with IB-MECA(see histology score in example 1C).

The difference between applicant's claimed method and the method of Fishman is that Fishman's do not disclose that the bone resorption that is treated is accelerated.

It would have been obvious to one having ordinary skill in the art, at the time the claimed invention was made, in view of Fishman, to treat bone resorption (bone loss) in a subject regardless of the type of bone loss or what induces the bone loss by administering to the said subject the A3AR agonist such as IB-MECA or CL-IB-MECA, since Fishman discloses that

A3AR agonist such as IB-MECA or CL-IB-MECA can be used to treat bone resorption (bone loss).

One having ordinary skill in the art would have been motivated in view of Fishman, to treat bone resorption (bone loss) in a subject, regardless of the type of bone loss or what induces the bone loss, by administering to the said subject an A3AR agonist such as IB-MECA or CL-IB-MECA, because a skilled artisan would reasonably be expected to use or administer A3AR agonist such as IB-MECA or CL-IB-MECA, to treat bone resorption (the same condition or disease) based on factors such as type and/or severity of the condition or disorder. It should be noted that the use of different schedules of administration or dosages are common in the art and is well within the purview of a skilled artisan and depends on factors such as the severity or type of the rheumatoid arthrithis and the weight, age and type of the subject treated. It should be noted that it is obvious to treat the said accelerated bone resorption (bone loss) regardless of what induces or causes the bone resorption (bone loss) and one of ordinary skill in the art would be motivated to treat accelerated bone resorption with said compound in said subject as set forth in the above rejection. That is, bone resorption or accelerated bone resorption is the same condition or disorder regardless of what induces or causes it.

Response to Arguments

Applicant's arguments with respect to claim 1,2, 5-10, 20 have been considered but are not found convincing.

The applicant argues that it is noted that the Fishman patent publication does not specify any particular histology score particularly for the bone damage so it is not clear from this publication what that particular score was in Example IC. However, the histology score which is

markedly decreased on treatment with said IB-MECA includes bone loss as indicated by parameter (e). In addition, it should be noted that Figs 3A and 3B show histological pictures of the joint of an untreated rat (3A), featuring the typical arthritis destruction of the synovial tissue and **bone** (see page 16, 2nd paragraph and said figures of Fishman). Against this the histological picture (3B) of adjuvant arthritis induced rat treated with 10 μg/kg a day of IB-MECA appeared completely normal without featuring any destructive processes (see page 16, 2nd paragraph and said figures of Fishman). This further indicates that IB-MECA reduces the bone loss or resorption.

The applicant argues that those of ordinary skill in the art reading the Fishman reference, if taught anything at all about the effect of IB-MECA or CI-IB-MECA on bone resorption when treating inflammatory arthritis patients, would only be taught that this is a side effect of the anti-inflammatory treatment. There certainly would be no suggestion that IB-MECA or CI-IB-MECA, or any other A3AR agonist, would be operable to treat accelerated bone resorption in diseases or conditions that are not related to inflammation. However, as set forth in the above rejection, Fishman reduces the bone loss (bone resorption) in a subject by administering to the subject IB-MECA. In addition, Fishman measures the loss of bone and reports that bone loss was markedly lower in the subjects treated with IB-MECA(see histology score in example 1C). Furthermore, the histology score which is markedly decreased on treatment with said IB-MECA includes bone loss as indicated by parameter (e). In addition, it should be noted that Figs 3A and 3B show histological pictures of the joint of an untreated rat (3A), featuring the typical arthritis destruction of the synovial tissue and **bone** (see page 16, 2nd paragraph and said figures of Fishman). Against this the histological picture (3B) of adjuvant

arthritis induced rat treated with 10 μg/kg a day of IB-MECA appeared completely normal without featuring any destructive processes (see page 16, 2nd paragraph and said figures of Fishman). This further indicates that IB-MECA reduces the bone loss or resorption. Moreover, it should be noted that it is obvious to treat the said accelerated bone resorption (bone loss) (as set forth in the above rejection) regardless of what induces or causes the bone resorption (bone loss) and one of ordinary skill in the art would be motivated to treat accelerated bone resorption with said compound in said subject as set forth in the above rejection. That is, bone resorption or accelerated bone resorption is the same condition or disorder regardless of what induces or causes it.

The applicant argues that submitted data shows that bone loss takes place as a result of osteoclast differentiation (osteoclasts are cells that are responsible for bone destruction and the formation of bone loss) and that CFI01 (A_3AR agonist) inhibits osteoclast formation by a down regulation of RANKL, thus preventing bone loss. Surprisingly, the effect of A_3AR on preventing bone resorption is based on a fact independent of its anti-inflammatory effect. This would certainly have not been obvious to anyone of ordinary skill in the art reading the Fishman reference. However, it should be noted that it is obvious to treat the said accelerated bone resorption (bone loss) (as set forth in the above rejection) regardless of the lack or absence of information that pertains to mechanism (s) by which the treatment occurs or regardless of what induces or causes the bone resorption (bone loss) and one of ordinary skill in the art would be motivated to treat accelerated bone resorption with said compound in said subject as set forth in the above rejection. That is, bone resorption or accelerated bone resorption is the same condition or disorder regardless of what induces or causes it.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Henry whose telephone number is 571-272-0652. The examiner can normally be reached on 8.30am-5pm; Mon-Fri. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia A. Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Michael C. Henry
November 23, 2008.

/Shaojia Anna Jiang/
Supervisory Patent Examiner
Art Unit 1623